

WHAT IS CLAIMED IS:

Subt B1
5 ~~1. A water-soluble luminescent semiconductor quantum dot, which comprises a core, a cap and a hydrophilic attachment group.~~

sub c2
2. The water-soluble luminescent semiconductor quantum dot of claim 1, wherein the hydrophilic attachment group is attached to said quantum dot via a sulfur atom.

10 3. The water-soluble luminescent semiconductor quantum dot of claim 2, wherein said hydrophilic attachment group is an organic group comprising a sulfur atom and at least one hydrophilic substituent.

15 4. The water-soluble luminescent semiconductor quantum dot of claim 3, wherein said hydrophilic substituent is selected from the group consisting of a carboxylic acid or salt thereof, a sulfonic acid or salt thereof, a sulfamic acid or salt thereof, an amino substituent, a quaternary ammonium salt, and a hydroxy.

sub c3
20 5. The water-soluble luminescent semiconductor quantum dot of claim 3, wherein said organic group is a C₁-C₆ alkyl group or an aryl group.

25 6. The water-soluble luminescent semiconductor quantum dot of claim 3, wherein said organic group is a C₁-C₆ alkyl group.

7. The water-soluble luminescent semiconductor quantum dot of claim 3, wherein said hydrophilic attachment group is a thiol carboxylic acid or thiol alcohol.

30 8. The water-soluble luminescent semiconductor quantum dot of claim 7, wherein said hydrophilic attachment group is mercaptoacetic acid.

⁶~~6~~. The water-soluble luminescent semiconductor quantum dot of claim 1, wherein the core of the quantum dot is selected from the group consisting of IIB-VIB semiconductors, IIIB-VB semiconductors, and IVB-IVB semiconductors and the size of the core is from about 1 nm to about 10 nm.

5 ⁷~~10~~. The water-soluble luminescent semiconductor quantum dot of claim ⁶~~9~~, wherein the core of the quantum dot is selected from the group consisting of IIB-VIB semiconductors and the size of the core is from about 2 nm to about 5 nm.

10 ⁸~~11~~. The water-soluble luminescent semiconductor quantum dot of claim ⁷~~10~~, wherein the core of the quantum dot is CdS or CdSe.

⁹~~12~~. The water-soluble luminescent semiconductor quantum dot of claim ⁸~~11~~, wherein the core of the quantum dot is CdSe.

15 ¹¹~~13~~. The water-soluble luminescent semiconductor quantum dot of claim ⁹~~12~~, wherein the size of the core is about 4.2 nm.

20 ¹²~~14~~. The water-soluble luminescent semiconductor quantum dot of claim 1, wherein the cap is selected from the group consisting of IIB-VIB semiconductors of high band gap.

¹³~~15~~. The water-soluble luminescent semiconductor quantum dot of claim ¹²~~14~~, wherein the cap is ZnS.

25 ¹⁰~~16~~. The water-soluble luminescent semiconductor quantum dot of claim ⁸~~11~~, wherein the cap is ZnS.

30 ¹⁴~~17~~. The water-soluble luminescent semiconductor quantum dot of claim ¹²~~14~~, wherein the cap is CdS.

¹⁵
~~18.~~ The water-soluble luminescent quantum dot of claim ⁹~~12~~, wherein the cap is CdS.

19. A water-soluble luminescent semiconductor quantum dot, which
5 comprises a CdSe core, a ZnS cap and a mercaptoacetic acid attachment group.

20. The water-soluble luminescent semiconductor quantum dot of claim 19,
wherein the CdSe core is about 4.2 nm and the ZnS coating is about 1 nm.

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10 ~~21.~~ A composition comprising the water-soluble luminescent semiconductor quantum dot of claim 1 and an aqueous carrier.

22. A composition comprising the water-soluble luminescent semiconductor quantum dot of claim 19 and an aqueous carrier.

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23. A composition comprising the water-soluble luminescent semiconductor quantum dot of claim 20 and an aqueous carrier.

¹⁷
20 ~~24.~~ A conjugate comprising the water-soluble luminescent semiconductor quantum dot of claim 1 and a biomolecule, wherein the biomolecule is attached to the quantum dot via the hydrophilic attachment group.

25. The conjugate of claim 24, wherein the biomolecule is a protein or a fragment thereof.

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26. The conjugate of claim 25, wherein the protein or fragment thereof is an antibody or an antigenically reactive fragment thereof.

27. The conjugate of claim 24, wherein the biomolecule is a nucleic acid.

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28. The conjugate of claim 24, wherein the biomolecule is attached to the hydrophilic attachment group via a linker.

29. A conjugate comprising the water-soluble luminescent semiconductor quantum dot of claim 19 and a biomolecule.

5 30. A conjugate comprising the water-soluble luminescent semiconductor quantum dot of claim 20 and a biomolecule.

31. The conjugate of claim 28, wherein the linker is a primary amine.

10 32. The conjugate of claim 28, wherein the linker is streptavidin, neutravidin or biotin.

33. The conjugate of claim 28, wherein the linker is a thiol group.

15 34. The conjugate of claim 28, wherein said biomolecule is a single-stranded oligonucleotide comprising a stem and loop structure and wherein said hydrophilic attachment group is attached to one end of the single-stranded oligonucleotide and a quenching moiety is attached to the other end of the single-stranded oligonucleotide and said quenching moiety quenches said luminescent semiconductor quantum dot.

20 35. A composition comprising the conjugate of claim 24 and an aqueous carrier.

25 36. A composition comprising the conjugate of claim 29 and an aqueous carrier.

37. A composition comprising the conjugate of claim 30 and an aqueous carrier.

30 38. A method of obtaining a water-soluble luminescent semiconductor quantum dot, which method comprises:

- (a) reacting a luminescent semiconductor quantum dot in a nonpolar organic solvent with a first aqueous solution comprising an attachment group;
(b) adding a second aqueous solution of about neutral pH and mixing; and
(c) extracting an aqueous layer, thereby obtaining a water-soluble luminescent semiconductor quantum dot.

39. The method of claim 38, wherein the nonpolar organic solvent is chloroform and the compound is mercaptoacetic acid.

40. A method of making a conjugate comprising a water-soluble luminescent semiconductor quantum dot of claim 1 and a biomolecule, which method comprises:

- (a) contacting a water-soluble luminescent semiconductor quantum dot of claim 1 with a biomolecule, which can directly attach to the attachment group on the cap of the water-soluble luminescent semiconductor quantum dot; and
(b) isolating the conjugate.

41. The method of claim 40, wherein said biomolecule is a protein or a fragment thereof or a nucleic acid.

42. The method of claim 40, wherein said attachment group is mercaptoacetic acid.

43. The method of claim 40, wherein (a) further comprises contacting the water-soluble luminescent semiconductor quantum dot and the biomolecule with a crosslinker.

44. A method of making a conjugate comprising a water-soluble luminescent semiconductor quantum dot of claim 1 and a biomolecule, which method comprises:

- (a) contacting a water-soluble luminescent semiconductor quantum dot of claim 1 with (i) a linker, an intermediate crosslinker or a bifunctional molecule, and then (ii) a biomolecule, which can indirectly attach to the

attachment group on the cap of the water-soluble luminescent semiconductor quantum dot; and

(b) isolating the conjugate.

5 45. The method of claim 44, wherein said biomolecule is a protein or a fragment thereof or a nucleic acid.

10 46. The method of claim 44, wherein said attachment group is mercaptoacetic acid.

47. The method of claim 46, wherein said linker is streptavidin, neutravidin or biotin.

15 48. A method of making a conjugate comprising a water-soluble luminescent semiconductor quantum dot of claim 1 and a biomolecule, which method comprises:

(a) contacting a biomolecule with (i) a linker, an intermediate crosslinker or a bifunctional molecule, and then (ii) a water-soluble luminescent semiconductor quantum dot of claim 1; and
(b) isolating the conjugate.

20 49. The method of claim 48, wherein said biomolecule is a protein or a fragment thereof or a nucleic acid.

25 50. The method of claim 49, wherein said attachment group is mercaptoacetic acid.

51. The method of claim 50, wherein said linker is streptavidin, neutravidin or biotin.

30 52. A method of detecting a protein in a sample, which method comprises:
(a) contacting the sample with a conjugate of claim 24, wherein the biomolecule of the conjugate specifically binds to the protein; and

(b) detecting luminescence, wherein the detection of luminescence indicates that the conjugate bound to the protein in the sample.

53. The method of claim 52, wherein the biomolecule of the conjugate is a protein or a fragment thereof.

54. The method of claim 53, wherein the biomolecule of the conjugate is an antibody or an antigenically reactive fragment thereof and the protein in the sample is an antigen or an epitope thereof that is bound by the antibody or the antigenically reactive fragment thereof.

55. The method of claim 54, wherein the antigen or the epitope thereof is viral or bacterial.

56. The method of claim 53, wherein the biomolecule of the conjugate is an antigen or an epitope thereof and the protein in the sample is an antibody or an antigenically reactive fragment thereof that binds to the antigen or epitope thereof.

57. The method of claim 56, wherein the antibody or the antigenically reactive fragment thereof is specific for a virus, a bacterium, a part of a virus, or a part of a bacterium.

58. The method of claim 52, wherein the biomolecule of the conjugate is a nucleic acid.

59. A method of detecting a nucleic acid in a sample, which method comprises:

(a) contacting the sample with a conjugate of claim 24, wherein the biomolecule of the conjugate specifically binds to the nucleic acid; and

(b) detecting luminescence, wherein the detection of luminescence indicates that the conjugate bound to the nucleic acid in the sample.

60. The method of claim 59, wherein the biomolecule is a nucleic acid.

61. The method of claim 59, wherein the biomolecule is a protein or a fragment thereof.

5 62. A method of detecting a nucleic acid in a sample, which method comprises:

10 (a) contacting the sample with a conjugate of claim 34, wherein said loop comprises a probe sequence that binds to a target sequence in said nucleic acid, whereupon the conjugate undergoes a conformational change that forces the stem to open, thereby separating the quantum dot moiety and the quenching moiety; and

15 (b) detecting luminescence, wherein the detection of luminescence indicates that the conjugate bound to the nucleic acid in the sample.

20 63. A method of detecting a nucleic acid in a sample, which method comprises:

25 (a) contacting a sample comprising a first single-stranded nucleic acid with a solid support to which is attached a second single-stranded nucleic acid that can bind to said first single-stranded nucleic acid; and

(b) contacting said solid support with a conjugate of claim 27, in which the biomolecule is a third single-stranded nucleic acid that specifically binds to the first-single stranded nucleic acid in a region other than that which is bound by the second single-stranded nucleic acid, and

30 (c) detecting luminescence, wherein the detection of luminescence indicates that the third single-stranded nucleic acid of the conjugate bound to the first single-stranded nucleic acid in the sample.

64. A method of detecting a nucleic acid in a sample, which method comprises:

- (a) attaching a nucleic acid capture probe to a solid support, wherein said nucleic acid capture probe comprises a sequence that binds to the nucleic acid in the sample;
- (b) contacting the attached nucleic acid capture probe with said sample, thereby immobilizing said nucleic acid on the solid support;
- (c) contacting the immobilized nucleic acid with a conjugate of claim 27, wherein the biomolecule of the conjugate specifically binds to the nucleic acid; and
- (d) detecting luminescence, wherein the detection of luminescence indicates that the conjugate bound to the nucleic acid in the sample.

65. A method of simultaneously detecting either two or more different molecules and/or two or more regions of a given molecule in a sample, which method comprises:

- (a) contacting the sample with two or more conjugates of claim 24, wherein each of the two or more conjugates comprises a quantum dot of a different size or composition and a biomolecule that specifically binds to a different molecule or a different region of a given molecule in said sample; and
- (b) detecting luminescence, wherein the detection of luminescence of a given color is indicative of a conjugate binding to a molecule in said sample.

66. The method of claim 65, wherein said sample comprises two or more different proteins or fragments thereof.

67. The method of claim 65, wherein said sample comprises two or more different nucleic acids.

68. The method of claim 65, wherein said sample comprises at least one nucleic acid and at least one protein or fragment thereof.